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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,826	12/19/2001	Hans-Georg Ihlenfeldt	BMID9918CUS	4203

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,826	IHLENFELDT ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2001* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/308,034* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *03/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

NON-FINAL ACTION

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. **This reference must be submitted during the pendency of the application, and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. This time period is not extendable (37 C.F.R. 1.78 (2).**

Specification

2. The preliminary amendment filed 05 March 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: New Claim 26 is drawn to an aqueous solution comprising dideoxynucleotide triphosphates. The specification as originally filed does not teach or describe the newly claimed solution. The specification repeatedly and solely

teaches solutions comprising nucleoside triphosphates (e.g. Examples 1-5). However, the specification does not teach or describe the solutions comprising dideoxynucleotides as newly claimed. As such, Claim 26 introduces new matter into the disclosure.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Claim 26 is drawn to an aqueous solution comprising dideoxynucleotide triphosphates. The specification as originally filed fails to define or provide support for the newly claimed solution. The specification repeatedly and solely teaches solutions comprising nucleoside triphosphates (e.g. Examples 1-5). However, the specification does not teach or describe the solutions comprising dideoxynucleotides as newly claimed. As such, the specification fails to define or provide support for the claimed invention.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 15 & 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Promega catalog (1992-1993, page 170) in view of Perkin Elmer Cetus (GeneAmp™ DNA Amplification Reagent Kit, 1988).

Regarding Claim 15, Promega teaches an aqueous solution containing one or more nucleoside triphosphates, wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances (page 170, Catalog No. U1240) wherein the solution is described at the Promega web site (http://egi.promega.com/catalog/catinfo.asp?idx=1018).

Regarding Claim 17, Promega teaches the solution wherein the pH is 7.5 (see web site description).

Regarding Claim 18, Promega teaches the solution wherein the concentration of said nucleoside triphosphates is between about 2 to 200 mmol/l (see web site description).

Regarding Claim 19, Promega teaches the solution wherein the nucleoside triphosphates are deoxynucleoside triphosphates (page 170).

Regarding Claim 20, Promega teaches the solution wherein the concentration contains a substance which buffers at pH 7.5 i.e. water (see web site description).

Promega teaches the claimed solution having a pH of 7.5 but does not teach the solution having a pH above 7.5. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the teaching of a pH of 7.5 encompasses minor variations in pH above the pH of 7.5 e.g. 7.5001. Alternatively, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5 (e.g. 7.5001) using routine experimentation to optimize solution conditions to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

7. Claims 16 & 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Promega catalog (1992-1993, page 170) in view of Gibco BRL catalog (1993, page 300).

Regarding Claims 16 & 26, Promega teaches an aqueous solution containing one or more nucleoside triphosphates, wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances (page 170, Catalog No. U1240) wherein the solution is described at the Promega web site (http://egi.promega.com/catalog/catinfo.asp?idx=1018) but Promega does not teach the nucleoside triphosphates are modified e.g. dideoxynucleotides. However, modified nucleoside triphosphates (e.g. dideoxynucleotides) in aqueous solutions were well known in the art at the time the claimed invention was made as taught by Gibco BRL. Specifically, Gibco BRL teaches a similar aqueous nucleoside triphosphate solution free from stabilizers wherein the nucleoside triphosphates are modified i.e. ddATP (page 300, Catalog No. 8243C). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleoside triphosphate of Promega with

the modified nucleoside triphosphates taught by Gibco BRL for the expected benefit of providing detectable nucleosides based on the modification e.g. termination of extension product. Additionally, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5 (e.g. 7.5001) using routine experimentation to optimize solution conditions to thereby maximize experimental results.

8. Claims 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Promega catalog (1992-1993, page 170) in view of Perkin Elmer Cetus (GeneAmp™ DNA Amplification Reagent Kit, 1988). The claims are drawn methods for replication nucleic acid fragments (Claim 21), synthesizing nucleic acid sequences (Claim 22), random priming of nucleic acid sequences (Claim 23), nick translation of nucleic acid sequences (Claim 24) and synthesizing nucleic acid sequences via a polymerase chain reaction (Claim 25). The claimed methods are acknowledged by applicant as known in the art wherein the improvement being the methods comprising the solution according to Claim 15. Promega teaches the claimed solution and the use of the claimed solution as detailed below. Perkin Elmer Cetus was not relied upon for the previous rejection but was merely cited for the teaching of methods which applicant acknowledged as known in the art.

Regarding Claim 21, Promega teach replicating nucleic acid fragments i.e. cDNA synthesis comprising the solution of Claim 15 wherein the pH is 7.5 (see web site description).

Regarding Claim 22, Promega teach synthesizing nucleic acid sequences i.e. sequencing comprising the solution of Claim 15 (see web site description).

Regarding Claim 23, Promega teach random priming i.e. sequencing comprising the solution of Claim 15 wherein the pH is 7.5 (see web site description).

Regarding Claim 24, Promega teach nick translation i.e. labeling comprising the solution of Claim 15 wherein the pH is 7.5 (see web site description).

Regarding Claim 25, Promega teach a solution containing one or more nucleoside triphosphates wherein the pH value of said solution is 7.5 and wherein said solution is free of stabilizing substances and wherein sequencing reactions comprise said solution (Catalog No. 1240, page 170 and web site description).

Promega teaches the solution having a pH of 7.5 but does not teach the solution having a pH above 7.5. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the teaching of a pH of 7.5 encompasses minor variations in pH including a pH above the pH of 7.5 e.g. 7.5001. Alternatively, it would have been obvious to one skilled in the art to modify the 7.5 pH of Promega to a pH above 7.5 (e.g. 7.51) using routine experimentation to optimize experimental conditions to thereby maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Additionally, the skilled practitioner in the art would have been motivated to apply the solution of Promega to methods known in the art and to raise the assay solution pH from 7.5 to above 7.5 based on the assay conditions taught by Perkin Elmer Cetus wherein the assay is performed in 25mM TAPS-Cl, pH 9.3 for the benefit of economy of time and reagent cost by eliminating the need to adjust the pH of the assay solution to maintain the desired pH of 9.3 and to thereby optimize experimental conditions and maximize experimental results

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
March 19, 2003